ISTANBUL TECHNICAL UNIVERSITY ★ GRADUATE SCHOOL OF SCIENCE ENGINEERING AND TECHNOLOGY

SELECTIVE SYNTHESIS OF MONO-SUBSTITUTED PENTAERYTHRITOLS VIA BICYCLIC NEUTRAL BORON ESTER FORMATION

M.Sc. THESIS

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Programı : Herhangi Program

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İSTANBUL TEKNİK ÜNİVERSİTESİ ★ FEN BİLİMLERİ ENSTİTÜSÜ

BİSİKLİK NÖTRAL BOR ESTER OLUŞUMU İLE SEÇİMLİ PENTAERİTRİTOL MONOESTERLERİ SENTEZİ

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Baris Kumru, a M.Sc. student of ITU Graduate School of Science Engineering and Technology, student ID 509141036, successfully defended the thesis entitled "SELECTIVE SYNTHESIS OF MONO-SUBSTITUTED PENTAERYTHRITOLS VIA BICYCLIC NEUTRAL BORON ESTER FORMATION", which he prepared after fulfilling the requirements specified in the associated legislations, before the jury whose signatures are below.

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Date of Submission : 03 February 2016
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To my mother and friends,

FOREWORD

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June 2016 Barış Kumru

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ABBREVIATIONS

^{1}H NMR	**:** Hydrogen Nuclear Magnetic Resonance
^{11}B NMR	**:** Boron 11 Nuclear Magnetic Resonance
^{13}C NMR	**:** Carbon 13 Nuclear Magnetic Resonance
DC	**:** Direct Current
DMSO- d6	**:** Deuterated Dimethyl Sulfoxide
FT-IR	**:** Fourier Transform- InfraRed
M	**:** Molar
Mesylate	**:** Methane Sulfonyl Ester
m.p.	**:** Melting Point
NMR	**:** Nuclear Magnetic Resonance
PETN	**:** Pentaerythritol Tetranitrate
pH	**:** Power of Hydrogen (Acidity-Basicity Term)
ppm	**:** Parts per Million

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SELECTIVE SYNTHESIS OF MONO-SUBSTITUTED PENTAERYTHRITOLS VIA BICYCLIC NEUTRAL BORON ESTER FORMATION

SUMMARY

By having four primary hydroxy groups, pentaerythritol has a compromising structure for further modifications. Tetraester, triester and diester modification of pentaerythritol have been reported in the literature previously, however monoesterification of this molecule has not been achieved with high yields and high purities so far. All the primary hydroxy groups in the molecule have exactly the same reactivity due to their same structure and same orientation. Selective monomodification of one of these hydroxy groups has been a key challenge for so long. This thesis aims to create well defined monoesterification procedure for pentaerythritol with high yields and high purities. Temporary blocking three hydroxy groups of pentaerythritol by forming neutral boron complex furnishes a convenient protocol for selective synthesis of mono substituted pentaerythritols via reaction of the residual methylol group. Tetracoordinated charged complex is sterically impossible in this case. Remaining only one active hydroxy group at the molecule yields monoesterification without the possibility of formation of poly substituted pentaerythritol. Molecule also orients itself downwards to yield complex with boron and pushes the free hydroxy group upwards which forms T-type like organic structure. Acylation of this free isolated hydroxy group yields boron containing liquid monoesters with relatively high yields. In order to retreive pentaerythritol monoesters, boron complex should be deesterified without damaging the carboxylic ester part. Boron ester moieties can be destroyed selectively by treating with 0.1 M HCl in ethanol solution in the presence of commercial anion exchanger, while retaining carboxylic ester unit unreacted. Selection of easy leaving carboxylic ester structures can also be used for further modifications in order to yield monosubstituted pentaerythritols. Monomesylated pentaerythritol-boron complex prepared by same way gives also monosubstituted pentaerythritols by action of strong nucleophiles. Solid monosubstituted pentaerythritol-boron complex can also be treated with acid in the necessary conditions discussed before to remove the boron from the structure. It is also interesting to note that water solubility of the structures is boron dependent; boron ester forms are water immiscible liquids and formation of three hydroxy groups makes it good water soluble. Boron release-uptake cycle is also reversible; acidic medium causes the deformation of boron structure whereas neautral or basic medium causes boron uptake from the three hydroxy structure. As outcome, well defined monoesters of pentaerythritol can be prepared with high yields and high purities, as it is also possible to keep the structure in the acyl-mesyl and bicyclic boron ester form. Nucleophilic substitution of monomesylated product yields monosubstituted pentaerythritols.

BİSİKLİK NÖTRAL BOR ESTER OLUŞUMU İLE SEÇİMLİ PENTAERİTRİTOL MONOESTERLERİ SENTEZİ

ÖZET

4 adet primer hidroksi grubuna sahip pentaeritritol, suda çözünen beyaz kristal yapıda bir maddedir. Hidroksi gruplarının reaktivitesi ve geometrik yapısı tamamen aynıdır. Pentaeritritol kendi başına birçok sanayi dalında katkı maddesi olarak kullanılır. Hidroksi gruplarını modifiye etmek ise uzun zamandan beri süregelmektedir. Bunun en rahat örneği esterleşme reaksiyonlarıdır. Serbest hidroksi grubunun açil klorürler ile reaksiyonu sonucu esterleşme gerçekleşir. Mineral asitlerin kullanılması ile de sübstitüye pentaeritritoller elde edilmektedir. Ancak 4 hidroksi grubunun eşit reaktivitede olması seçici bir şekilde mono, di ya da trimester sentezini zorlaştırmaktadır. Literatürde yaygın olarak pentaeritritolün tetraesterleri bulunmaktadır. Pentaeritritol tetraakrilat, ultraviyole (UV) ışık kullanımında iyi bir çapraz bağlayıcı ve kürleme ajanıdır. Sentezi için ise pentaeritritol; aşırı miktarda akriloil klorür ile muamele edilir ve serbest hidroksilerin tümünün reaksiyona girmesi zorlanmış olur. Pentaeritritolün tetranitrat esteri ise uzun zamandan beri bilinen iyi bir patlayıcıdır. Aşırı miktardaki nitric asidin asit katalizliğinde pentaeritritol ile reaksiyonu sonucu elde edilir. Yapısal olarak nitrogliserine benzemektedir ve yüksek nitro grubu ihtiva etmesinden dolayı patlayıcı özelliği keşfedilmiştir. Organik çözücülerde çözünmektedir. Doğada ise nitrat bakterileri sayesinde biyobozunuma uğramaktadır. Yapılan son çalışmalarda da tetrahekzanoik esterinin çok iyi miktarda karbon dioksit çözdüğü, ve bu sebeple bu malzemenin çok iyi bir karbon dioksit tutucu olarak kullanılabileceği anlaşılmıştır. Ayrıca halojen içermeyen bazı esterlerin iletkenlik özelliği taşıdığı ve bu maddelerin de mikroelektronik sistemlerde yaygın olarak kullanılabileceği öngörülmektedir.

Bahsedildiği üzere yapılan çalışmaların çoğunda elde edilen ürünler pentaeritritolün tetraesterleridir ve bu maddeler incelenmiştir. Aynı yaklaşım ile pentaeritritolün daha az sübstitüye esterleri elde edilememektedir. Pentaeritritolün diesterlerinin eldesi için 2 adet hidroksi grubu siklik asetal oluşturularak koruma altına alınır. Serbest kalan 2 adet hidroksi grubu üstüne gerekli modifikasyonlar yapılır ve en son olarak siklik asetal yapısı bozularak seçici olarak pentaeritritolllerin diesterlerinin sentezi mümkün olmuştur. Ancak seçici olarak mono ve triester sentezi halen tam olarak aydınlatılamamıştır. Örneğin monoester elde etmek istendiği zaman teorik olarak açil klorürlerin pentaeritritol ile molar eşit miktardaki reaksiyonu sonucu pentaeritritol monoester elde edilmesi gerekmektedir. Ancak, tüm hidroksi gruplarının eşit reaktivitesi bu durumda büyük sorun yaratmaktadır ve reaksiyon sadece monoester vermek yerine tüm olası sübstitüye esterleri vermektedir. Aynı sorun pentaeritritol trimester sentezi için de geçerlidir, bu durumda da trimester ve tetraester karışımları elde edilmektedir. Monoesterleşme reaksiyonunun daha çok karma ürün vermesi, pentaeritritol monoesterlerinin literatüre yabancı kalmasına sebep olmuştur. Bunun dışında seçici monoester sentezi herhangi bir organik sentez yaklaşımı henüz bulunmamaktadır. Belki de bu sebeplerden dolayı, literatürde genellikle pentaeritritolün tetraesterleri ve o kadar sık olmasa da diesterleri kolay sentezleri

bakımından karşımıza çıkmaktadır. Monoesterlerin günümüzde bilinen tek eldesi bahsedildiği üzere açil klorürün pentaeritritol ile molar denklikte reaksiyonu ve ardından kromatografik teknikler kullanılarak oluşan izomerlerin ayrılması şeklindedir. Bu da monoester eldesini zahmetli ve verimi düşük hale getirmektedir.

Yapılan tez çalışmasında, seçici olarak pentaeritritolün monoesterlerinin yüksek verim mesi ve saflıkta elde edilmesi hedeflenmiştir. Bu amaçla ilk olarak pentaeritriol, boric asit ile saf su içerisinde muamele edilmiş ve tam çözünme gözlenene kadar ısıtılmıştır. Ardından reaksiyon ortamına toluene ilavesi ile suyun tamamı Dean-Stark aparatı ile uzaklaştırılır. Elde edilen katı beyaz kristal yapının 3 koordinasyonlu nötral bor esteri olduğu anlaşılmıştır. 4-koordinasyonlu yüklü kompleks oluşması sterik olarak imkansızdır ve yapının iletkeliğinin olmaması da 3 koordinasyonlu nötral ester yapısını kanıtlamıştır. Yapının ayrıca suda stabilitesini aydınlatmak için ^{11}B NMR analizleri sonucu integral alanlardan bozunma miktarı hesaplanmıştır. Yapının geometrik olarak yönlenmesi sonucu komplekse katılan 3 adet hidroksi grubu bor ile birlikte yapının alt kısmına yönlenirken serbest hidroksi grubu ise yapının üst kısmına doğru yönlenmektedir.

Serbest tek hidroksi grubu barındıran bor kompleksi ardından açil klorürler ile baz varlığında reaksiyona tabi tutulur. Reaksiyonun saflaştırılması da bu bakımdan önemlidir. Reaksiyon tamamlandıktan sonar buzlu suya dökülür ve organik faz eklenir. Oluşabilecek diğer ürünler ve reaksiyona girmeyen maddelerin hepsi su fazında kalır ve organic faza sadece monoesterleşmiş bor kompleksli ürün geçer. Bu bağlamda reaksiyonun hem saflaştırılması kolaydır hem de tek hidroksi grubu bulunduğu için verimi yüksektir. Çalışmada elde edilen 5 tip bor kompleksli monoester yapılarının oluştuğu da analiz sonuçları ile kanıtlanmıştır. Oluşan ürünler organic sıvılardır ve su ile karışmazlar. Bu ürünlerin suda stabilitesi de merak konusu olmuş ve çeşitli yöntemler ile bu stabilite kontrol edilmiştir. Organik ürünlerin saf suda 7 güne kadar bozunmadan kaldığı ve ardından oluşan bozunma ile fazing kaybolduğu gözlenmiştir.

Pentaeritritol monoester eldesi için ise borun yapıdan uzaklaştırılması gerekmektedir. Mineral asitlerin alkol çözeltisi ile bor kompleksli pentaeritritol monoesterleri, ticari anyon değiştiriciler varlığında reaksiyona tabi tutulduğu zaman borun yapıdan uzaklaştığı ve karboksilik esterin bozunmadan kaldığı anlaşılmıştır. Çözücünün uzaklaştırılması sonucu elde edilen pentaeritritol monoesterleri katıdır ve 3 adet hidroksi grubu barındırdığından suda çözünür hale gelirler. Ayrıca, bor tutma-bırakma prosesinin tersinir olduğu anlaşılmıştır. Yani asidik ortamda bor esteri bozunurken bazik ve nötral ortamda borun tekrar yapıya katıldığı gözlemlenmiştir. Bu tersinir proses ise yapıların çözünürlük farkından dolayı rahatlıkla göz ile de takip edilebilmektedir. Suya bor kompleksli pentaeritritol monoesteri ilave edilir ve dipte organic faz oluşumu gözlenir. Asit ilavesi ile organik fazın kaybolduğu görülür ve baz ilavesi ile tekrar faz oluşumu gözlenir. Pentaeritritol monoesterleri ise yüksek erime noktasına sahip katılardır. Monomesil esteri ise asit ile muamele edildiğinde mesil grubunun da asit hidrolizine uğraması sonucu pentaeritritolün kendisi elde edilir.

Bor kompleksli pentaeritritol monomesil esteri ise bu çalışmada elde edilen diğer esterlerden farklı bir özellik taşımaktadır. Mesil grubunun kolay ayrılan grup özelliği taşıması sebebiyle bu grup ta daha ileri seviyede modifiye edilebilmektedir. Bu esterin organic çözücüde güçlü nükleofiller ile reaksiyonu sonucu monosübstitüye pentaeritritolün bor kompleksi elde edilmektedir. Bu sefer bor kompleksi halinde olan ürünler de katıdır. Boru yapıdan uzaklaştırmak için daha önce bahsedilen proses

uygulanır ve monosübstitüye pentaeritritoller elde edilir. Bor kompleksli ürünler suda çözünmezler ancak bor yapıdan çıkarıldığı zaman suda çözünür hale gelirler. Bor tutma-bırakma prosesi bu maddeler için de tersinir olarak gerçekleşmektedir.

Bu çalışmada keşfedilen proses ile pentaeritritolün 3 adet hidroksi grubunun bor ile bisiklik yapıda ester oluşturması ve geçici olarak korunması sağlanır. Bu bağlamda yönlenen molekül reaksiyon vermemiş tek hidroksi grubunu yapının üstüne yönlendirir. Serbest kalan hidroksi grubu üstünde esterleşme reaksiyonları yapılabilir. Yapıdan boru uzaklaştırmak ise asit muamelesi ile karboksilik esteri bozmadan gerçekleşir. Bu proses tersinirdir. Ayrıca monomesil esteri nükleofiller ile muamele edildiğinde yer değiştirme reaksiyonu gerçekleşir ve bu ürünlerden de borun ayrılması sonucu monosübstitüye pentaeritritoller elde edilir. Önerilen proses seçici olarak pentaeritritol monoesteri eldesine yöneliktir ve yüksek saflıkta ve yüksek verimde ürünler elde edilir.

1. INTRODUCTION

Pentaerythritol is a white crystalline solid having four primary hydroxy groups. This compound is water soluble (25 %) and melts at 263 ^{o}C. It finds various applications in manufacturing of intumescent flame retardent materials, wherein pentaerythritol acts as chare forming component [1-3]. Pentaerythritol find also application in production of alkyd resins [4] and lubricants [5]. Cyclic polyacetals and polyspyroketals of pentaerythritol derived from dialdehydes and cylohexanedione are widely used as hot-melt adhesive [6-8].

Tetraacrylate or methacrylate derivatives of pentaerythritol are known as radiation curing monomers [9]. Its tetranitrate ester (PETN) is structurally similar to trinitroglycerol (glycerol trinitrate). Therefore PETN is a very powerful explosive that was used in the first and second world wars [10-11].

Recently tetraesters of pentaerythritol with hexanoic acid have been demonstrated to dissolve large amonunts of carbon dioxide [12-13]. Such a high carbon dioxide affinity makes it promising for sequestering of this gas.

Complete modification or substitution of four hydroxyl groups of pentaerythritol is straightforward that could be achieved by using excess reagents. For instance tetraesters or tetrahalides of pentaerythritol can be obtained in good yields by using excess acid or hydrogen halide. However; preparation of the mono-, di-, and tri-esters of pentaerythritol is problematic and needs special procedures as reported by Barth and Burrell [14]. Similar attempt to prepare monobromine of pentaerythritol by action with hydrobromic acid (HBr) gives 65 % of monobromide and 16 % of dibromide and 18.5 % tribromide [15]. Despite tremendous efforts there appear no method providing pure mono-, di- or tri substituted pentaerythritol, so that there remains only tedious chromatographic techniques for the separation of isomers.

2. EXPERIMENTAL PART

^{1}H NMR and ^{13}C NMR were taken in deuterated dimthylsulfoxide (DMSO-d_6) solvent using Agilent VNMRS 500 MHz spectrometer at 298 K. ^{11}B NMR were taken in the same instrument using deuterated water (D_2O) solvent at 298 K. Fourier transform Infrared (FT-IR) spectra were recorded using Perkin Elmer FT-IR spectrum One B spectrometer at 298 K. Conductometry measurements were recorded using DDBJ-350 portable conductometer.

Herein we describe a boron ester orienting method for the selective synthesis of carboxylic and sulfonic acid monoesters of pentaerythritol in high yields. This method simply relies on blocking of three hydroxyl groups of pentaerythritol with boric acid by forming neutral boron ester (Figure 2.1). Involment of fourth methylol group in boron complexation to give tetracoordinated boron ester is almost impossible sterically. In the case of tetra-coordination, it is known that, anionic borate ester is accompanied by a proton making the complex strong acidic. Therefore, a sudden pH drop is expected for the tetra coordination. However, no change was measured in pH of the aqueous solution (pH: 6.4) of 1:1 boron- pentaerythritol mixture. This eliminates possibility of tetra coordination of boron with pentaerythritol.

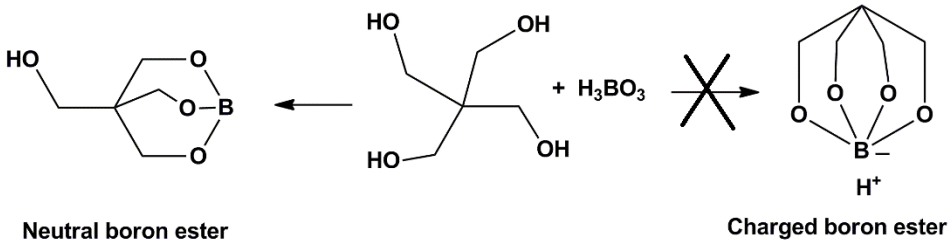


Figure 2.1 : Action of boric acid on pentaerythritol gives neutral 1:1 complex with one residual hydroxy group

In ^{1}H NMR spectrum of the boron complex (Figure A.1); methyleneoxy protons bicyclic structure exhibits one symmetrical doublet of doublet (J = 8.5 Hz) centered at 3.75 ppm, while methylol group gives a singlet at 3.32 ppm as expected (Figure 2.2). ^{13}C NMR spectrum of this compound (Figure A.11) exhibits three type of carbon. Methyleneoxy carbons and tertiary carbon signals appear at 70 and 69 ppm

respectively. The signal at 38 ppm must be due to methylol carbon. Figure A.23 shows the FT-IR spectrum of the initial complex. This compound is water soluble, but shows a reasonable hydrolytic stability as inferred from ^{11}B NMR spectrum taken in D_2O soon after its preparation in Figure 1c. On contrary to one singlet at -13 ppm, the spectrum taken after 36 h of contacting with D_2O shows a weak additional signal at + 16 ppm as seen in Fig 1d. Obviously the first peak must be ^{11}B signal of the boron ester whereas the last peak must be associated with ^{11}B signal of boric acid formed by hydrolysis [16]. Integral ratio of the two implies nearly 25 % of hydrolysis.

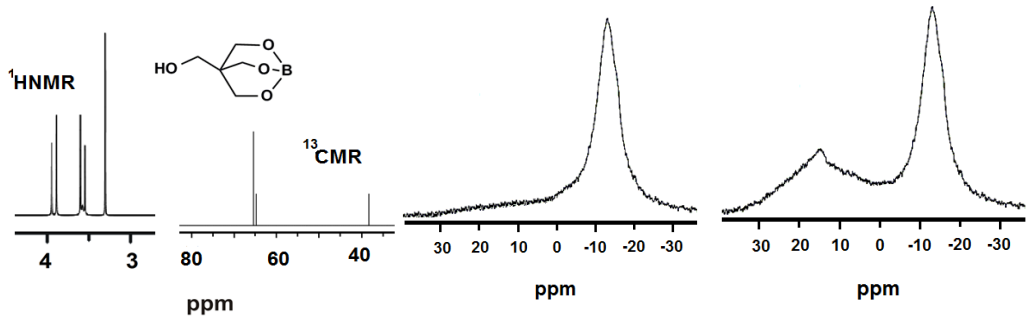


Figure 2.2 : ^{1}H NMR and ^{13}C NMR spectrum of 1:1 boron- pentaerythritol, complex (taken in DMSO- d6 (left). ^{11}B NMR spectrum of fresh pentaerythritol-boron complex (middle), after waiting for 2 days in D_2O (right).

Those results confirm that three hydroxy groups of pentaerythritol forms a neutral boron ester and one hydroxy group remains unreacted. It was concluded that this free hydroxy group can be further functionalized without destruction of the boron ester. Mild hydrolysis of the boron ester would give only monosubstituted pentaerythritol.

In the present work, esterification was chosen for the further reaction with the residual hydroxy group. A typical procedure was performed as follows. In a 250 mL of round bottom flask equipped with a Dean-Stark trap and a reflux condenser, there was added 13.6 g (0.1 mol) pentaerythritol, 6.1 g (0.1 mol) boric acid and 60 mL water. Then 40 mL of toluene was added to the mixture for azeotropic removal of water. The flask was mounted in an oil bath and heated at 120 ^{o}C, until all water was collected (~63 mL) in the reservoir of Dean-Stark trap. Then toluene was evaporated completely. The resulting white product was dry enough to use in the followed reaction with carboxylic and sulfonic acid chlorides.

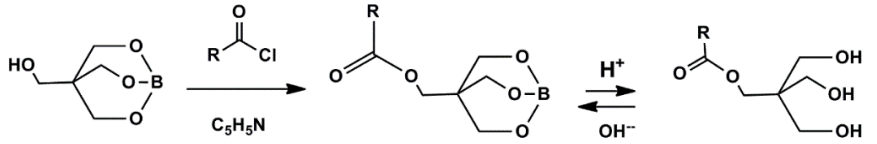
For the formation of monoesters, in the second step, in a 100 mL flask, 7.2 g (0,05 mole) boron containing complex was dispersed in 20 mL of acetone. Then, 4.0 g (0,05 mole) of pyridine is added for trapping of hydrochloric acid (HCl) evolved. The flask

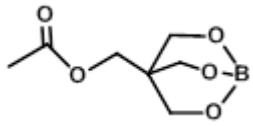
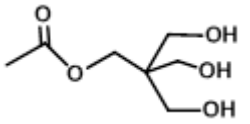
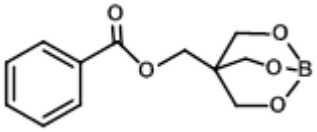
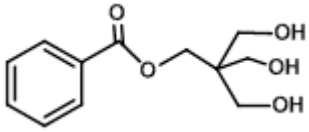
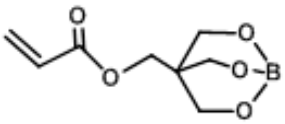
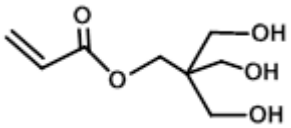
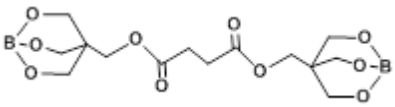
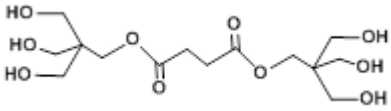
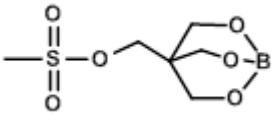
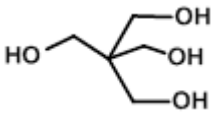
is placed into an ice bath and 0,05 mole of acyl chlorides (acetyl, benzoyl, adipoyl, acryloyl and mesyl chlorides) was added dropwise while stirring vigorously. Reaction is heated to 50 ^{o}C for 2 h. The only difference in the reaction with acryloyl chloride was addition of trace (0.1 g) hydroquinone to avoid polymerization of the double bonds during the condensation. After cooling the reaction mixture, it was poured into icy water and organic phase was extracted with dichloromethane (CH_2Cl_2). The organic phase dried with sodium sulfate (Na_2SO_4) and passed through basic alumina column (5x1). Evaporation of dichloromethane simply gives boron esters of pentaerythritol monocarboxylic acid esters (Table 2.1). Their related analysis results can be found on Supporting Results part. ^{1}H NMR spectrums of boron chelated pentaerythrtitol monoacetate (Figure A.2), boron chelated pentaeryhtritol monoacrylate (Figure A.3), boron chelated dipentaerythrtitol monoadipoate (Figure A.4), boron chelated pentaerythritol monobenzoate (Figure A.5) and boron chelated pentaerythritol monomesylate (Figure A.6) show the proof of the proceeding products. Figure A.12 and 4.13 show the characteristic ^{13}C NMR of the boron chelated pentaerythritol monoacetate and monomesylate diagrams to show the different type of carbons in different boron chelated monoesters. The characteristic FT-IR peaks can be seen for each compund; for boron chelated pentaerythritol monoacetate (Figure A.24), boron chelated pentaerythritol monoacrylate (Figure A.25), boron chelated dipentaerythritol monoadipate (Figure A.26), boron chelated pentaerythritol monobenzoate (Figure A.27) and boron chelated pentaerythritol monomesylate (Figure A.28) which show the identical peaks related to organic compounds. Boron ester peaks can be observed in each one of them.

Interestingly, the resulting cyclic boron chelates with ester groups are water-immiscible liquids and hydrolytically stable in neutral and slightly basic media. It was demonstrated that, boron ester moieties can be destroyed selectively by treating with 0.1-0.2 M HCl solution, while retaining carboxyl ester units unreacted. This process is reversible; so that shaking acetylated boron ester (1 mL) with a mixture 1 mL HCl solution (0.1 M) with 2 mL water in a glass tube results in disappearance of organic phase implying decomposition of the boron ester. Addition of 1-1.5 mL sodium hydroxide (NaOH) (0.1 M) restores the organic phase, which indicates reversibility of the boron chelation.

Existence of commercial anion exchanger during boron removal process is necessary due to complete removal of boron ions from the solution.

Table 2.1 : The practical yields of mono-esterification of pentaerythritol-boron complexes and yields of boron free pentaerythritol-carboxylic or methane sulfonic acid monoesters.



Entry	*Reagent*	*Boron containing ester*	*Pentaerithritol monoester*
1	Acetyl chloride	 Colorless liq (92 %)	 White solid (81 %) (m.p: 123 ± 0.8 °C)
2	Benzoyl chloride	 Colorless liq (91 %)	 White solid (87 %) (m.p: 105 ± 0.7 °C)
3	Acryloyl chloride	 Colorless liq (87 %)	 White solid (82 %) (m.p: 161 ± 1.2 °C)
4	Adipoyl chloride	 White solid (84 %)	 Powder (78 %) (m.p: 226 ± 0.4 °C)
5	Methane sulfonyl chloride	 Colorless liq (90 %)	 White powder (85 %)

In order to isolate boron-free monoesters we have studied precipitation of boric acid by salt forming with zinc (II) chloride ($ZnCl_2$) solution or calcium chloride ($CaCl_2$) solution after decomposing the boron complex by acid treatment. However, this was not successful to remove boric acid. The best procedure was mixing of acidified alcohol-water mixture with commercial anion exchange resin (Amberjet 4600). Amount of the resin (nearly 2 $mmolg^{-1}$) used was about 50 % excess.

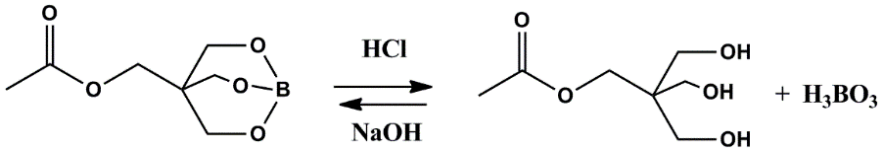


Figure 2.3 : Reversible boron releasing and binding by acid and base treatment

The boron-free monoesters were obtained by evaporating the solvent mixture after acid treatment (Figure 2.3). The products were high melting white solids. The solid samples (50-80 mg) did not give solid residue upon combustion by flame ignition on a hot plate, implying absence of the boric acid. The process repeated for each boron chelated monoesters to remove the boron from the structure. ^{1}H NMR spectrums for pentaerythritol monoacetate (Figure A.15), pentaerythritol monoacrylate (Figure A.16), dipentaerythritol monoadipate (Figure A.17) and pentaerythritol monobenzoate (Figure A.18) show the dissappearance of the doublet of doublet peaks and forms new type of proton signals.

Although boron containing carboxylic esters easily hydrolyze by dilute acids, they show good hydrolytic stability against neutral water. To estimate extent of hydrolysis while contacting with neutral water, biphasic mixture of 5 mL of monoacetyl ester of pentaerythritol-borate ester with 20 mL water was shaken for 1.0 min and left to stand for one week. To inspect amounts of boric acid formed by hydrolysis, 2.0 mL sample was taken from aqueous phase in every 24 h and mixed with 23.0 mL of 0.1 M sorbitol. Then DC conductivities and pHs of the solutions were measured and drawn against time (Figure 2.4). The conductivity of the solution stays nearly constant at 200 μS cm^{-1} but shows a sudden rise after seven days. Similarly significant decrease in pH after 7 days, imply up to seven days of stability in contacting with tap water.Sorbitol forms a charged complex structure with free boron in solution and thus it is a good method for the determination of free boron ions. It is a simple method due to reproducibility and ease of instrument.

The resulting products were freed from boron to obtain mono-substituted pentaerythritols. This was achieved by action of dilute mineral acid. In a typical procedure 2 mL of acetylated boron ester of pentaerythritol, 2 mL concentrated HCl solution and 18 mL methanol was mixed and stirred for 30 min at room temperature. Four grams of commercial anion exchange resin was introduced to the mixture to remove boron as borate anion. After shaking the mixture for 30 min, the mixture was filtered and the filtrate was heated to dryness by a rota evaporator.

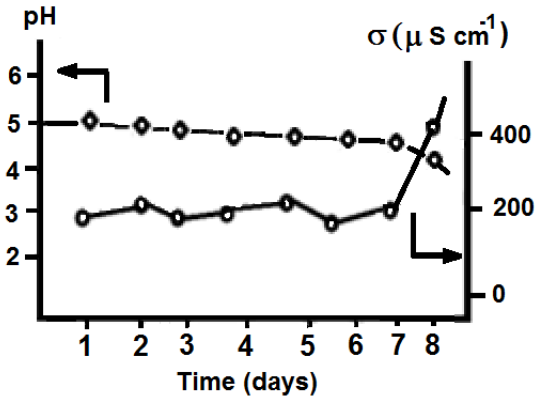


Figure 2.4 : Variation of pH and conductivity of water phase as a function of contact time of acetylated pentaerythritol boron ester

This process gives monocarboxylic esters of pentaerythritol as hygroscopic white powder (Table 2.1). FT-IR spectrums of pentaerythritol monoacetate (Figure A.33), pentaerythritol monoacrylate (Figure A.34), dipentaerythritol monoadipate (Figure A.35) and pentaerythritol monobenzoate (Figure A.36) indicates the existence of strong –OH peak formation which is due to destruction of boron ester group.

Structural changes of the products are readily followed by representative NMR spectra given in Figure 2.5 for acetate ester.

This component shows a doublet of doublet for methyleneoxy protons of the bicyclic ring in 3.4-3.9 ppm. The singlet methyleneoxy protons marked with c appears at 4.05 ppm. After hydrolysis of the boron complex quartet of the first peak disappears and methylol signals give a singlet at 3.3 ppm. Due to fruitful purification process, all possible impurities will be in water phase and organic phase is expected to only retreive the organic ester product. NMR spectra yields only expected signals due to organic ester structures, and the absence of unexpected peaks shows also the purity of the synthesized materials.

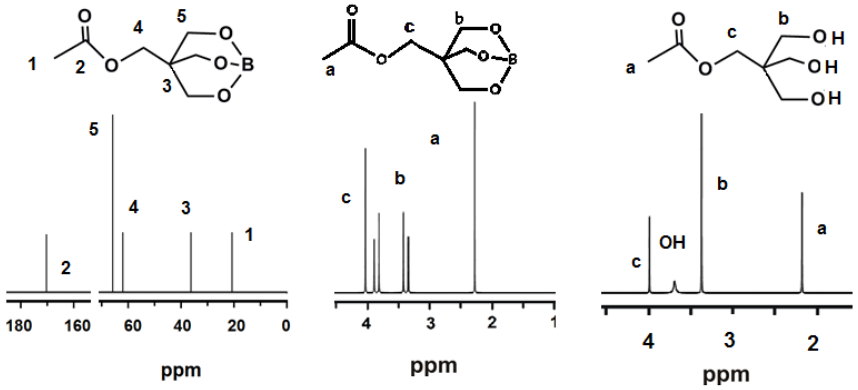


Figure 2.5 : ^{13}C NMR and ^{1}H NMR spectra of monoacetylated pentaerythritol-boron complex (left and middle) and its boron free derivative (right)

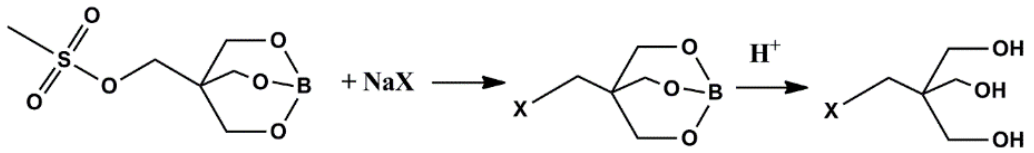
It is important to note that esterification of methylol group of pentaerythritol-boron complex can also be achieved by methane sulfonyl chloride. The acetone is removed from the mixture by evaporation, the residue left was mixed with 25 mL CH_2Cl_2. To remove pyridine salts the organic phase was washed with ice-water twice (2x50 mL) and separated. The liquid product was isolated after drying of the solution with anhydrous Na_2SO_4 (approx. 3.0 g) and evaporation of the solvent. The yield of this process is 75.6 %. It is important to note that CH_2Cl_2 is the best solvent to extract the product from the aqueous mixture, otherwise considerably low yields are attained.

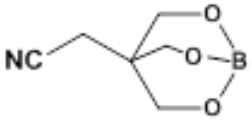
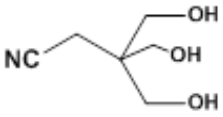
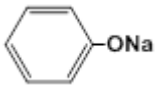
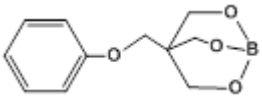
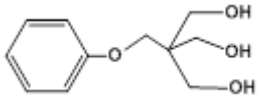
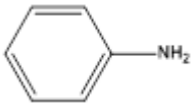
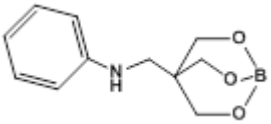
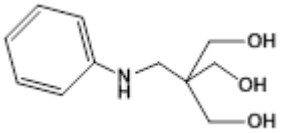
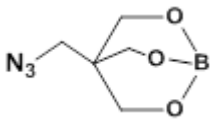
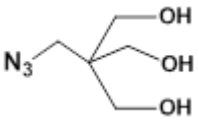
However boron free form of the resulting methane sulfonate (mesylate) cannot be obtained using dilute mineral acid, because mesyl group also undergoes hydrolysis to give naked pentaerythritol (Table 2.1).

The mesyl group, however, can be used for further modification by substituting with cyanide, phenolate or azide ions in N-methyl pyrrolidone solvent. In this reaction, 0,05 mole of mesylated pentaerythritol-boron ester was treated for 4 h with 0,05 mole of sodium cyanide (NaCN), 0,05 mole of sodium phenolate, 0,1 mole of aniline or 0.05 mol sodium azide (NaN_3) at 70 ^oC in the presence of N-methyl pyrrolidone. The solid products obtained by filtration after the reaction mixture is pored into water. Boron ester moieties of the resulting products are stable in neutral and slightly basic media, but they are readily hydrolyzed by treating with 0.1-0.2 M HCl solution and give monosubstituted pentaerythritols as listed in Table 2.2. ^1H NMR spectrums of boron chelated monocyano substituted pentaerythritol (Figure A.7), boron chelated monophenolate substituted pentaerythritol (Figure A.8), boron chelated monoazide substituted pentaerythritol (Figure A.9) and boron chelated monoaniline substituted pentaerythritol (Figure A.10) show the necessary peaks related to identical parts of the compunds. FT-IR spectrums of boron chelated monocyano substituted pentaerythritol (Figure A.29), boron chelated monophenolate substituted pentaerythritol (Figure A.30), boron chelated monoaniline substituted pentaerythritol (Figure A.31) and boron chelated monoazide substituted pentaerythritol (Figure A.32) show the boron ester peaks in each compound and significantly different peaks relate to their different structures. ^1H NMR spectrums of monocyano substituted pentaerythritol (Figure A.19), monophenolate substituted pentaerythritol (Figure A.20), monoaniline substituted pentaerythritol (Figure A.21) and monoazide substituted pentaerythritol (Figure A.22) show the absence of bicyclic ring protons and new peaks are formed due to destruction of boron ester while retaining the monosubstituted groups. FT-IR

spectrums of monocyano substituted pentaerythritol (Figure A.37), monophenolate substituted pentaerythritol (Figure A.38), monoaniline substituted pentaerythritol (Figure A.39) and monoazide substituted pentaerythritol (Figure A.40) show the –OH peak formations.

Table 2.2 : Reactions of mesylated pentaerythritol-boron complex for selective synthesis of mono-substituted pentaerythritols.



Run	*Reagent*	*Monosubstituted pentaerythritol-boron complex*	*Boron free Monosubstituted pentaerythritol*
1	**NaCN**	 Yellowish solid (61%)	 White solid (76 %) (m.p: 213 ±0. 5 ºC)
2		 Colorless solid (78%)	 White solid (77 %) (m.p: 193 ± 0.4 ºC)
3		 Brownish solid (79%)	 Brownish solid (m.p: 127 ± 1.1 ºC)
4	**NaN_3**	 Colorless solid (72 %)	 White solid (m.p: 187 ± 1.9 ºC)

3. CONCLUSION

As a result, action of boric acid on pentaerythritol gives neutral boron ester and one methylol group left unreacted. This group can be esterified with carboxylic acid chlorides. Treating with dilute mineral acid selectively hydrolyzes the boron ester and gives monoesterified pentaerithritols. The methylol group can also be sulfonated without decomposing the boron ester moiety. The sulfonate group can be used to obtain monosubstituted pentaerythritols selectively by nucleophilic substitution. Further investigations by our group will include the synthesis of pentaerythritol monomethacrylate as novel monomer, its polymerization, gelation and immobilization onto solid surfaces for advanced boron removal processes.

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APPENDICES

APPENDIX A: Figures

APPENDIX A

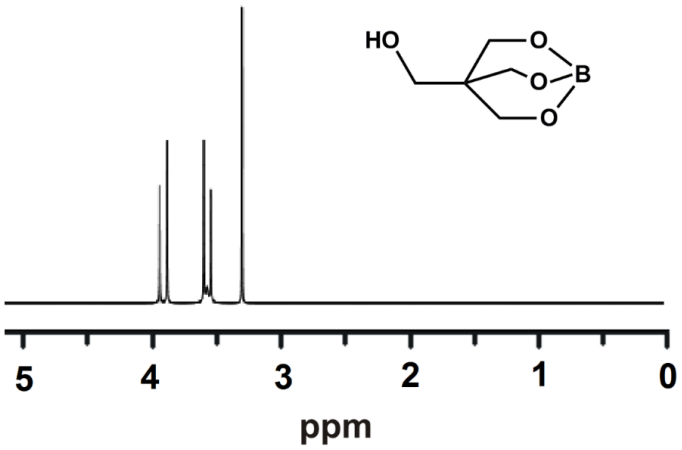

Figure A.1 : ^{1}H NMR Spectrum of boron chelated pentaerythritol [2,6,7-trioxa-1- borabicyclo[2.2.2]octan-4-ylmethanol]

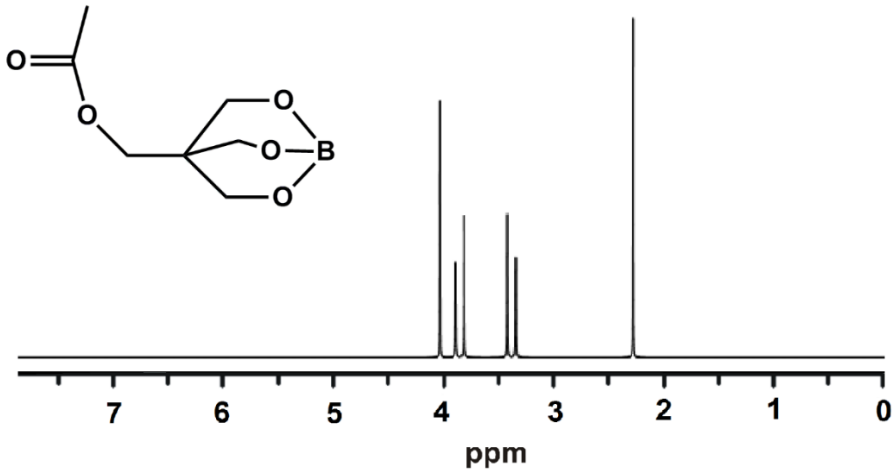

Figure A.2 : ^{1}H NMR Spectrum of boron chelated pentaerythritol monoacetate [2,6,7-trioxa-1-borabicyclo[2.2.2]octan-4-ylmethyl acetate]

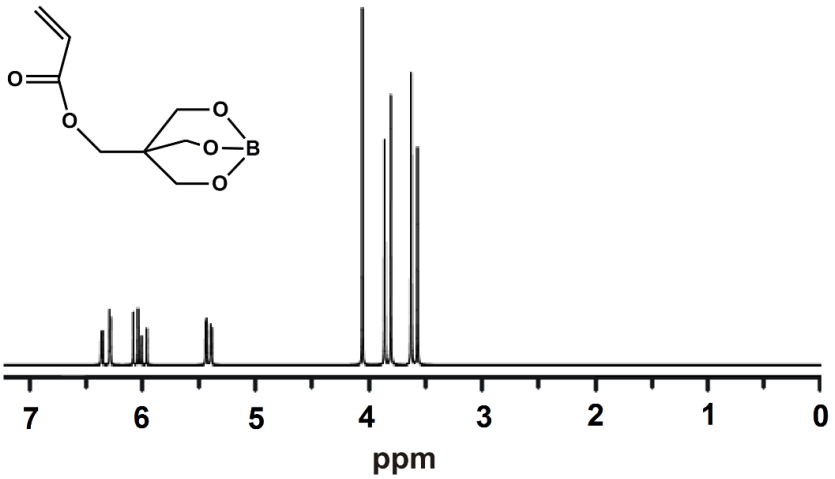

Figure A.3 : ^{1}H NMR Spectrum of boron chelated pentaerythritol monoacrylate [2,6,7-trioxa-1-borabicyclo[2.2.2]octan-4-ylmethyl acrylate]

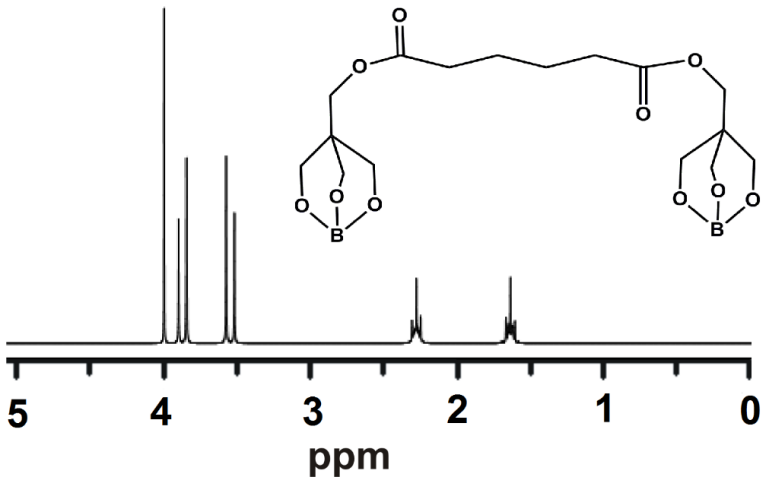

Figure A.4 : ^{1}H NMR Spectrum of boron chelated dipentaerythritol monoadipate [bis(2,6,7-trioxa-1-borabicyclo[2.2.2]octan-4-ylmethyl) adipate]

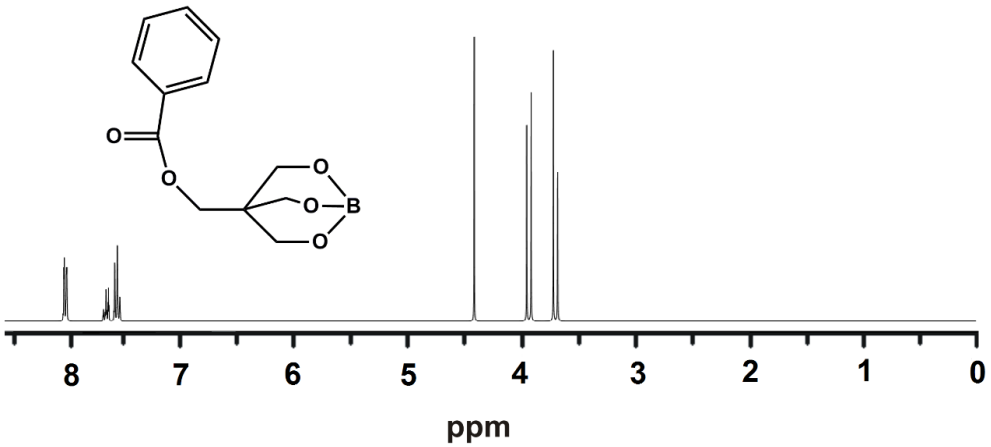

Figure A.5 : ^{1}H NMR Spectrum of boron chelated pentaerythritol monobenzoate [2,6,7-trioxa-1-borabicyclo[2.2.2]octan-4-ylmethyl benzoate]

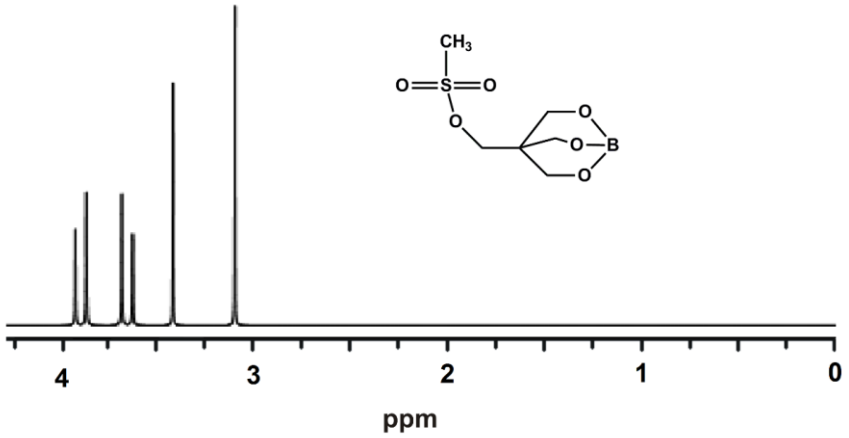

Figure A.6 : ^{1}H NMR Spectrum of boron chelated pentaerythritol monomesylate [2,6,7-trioxa-1-borabicyclo[2.2.2]octan-4-ylmethyl methanesulfonate]

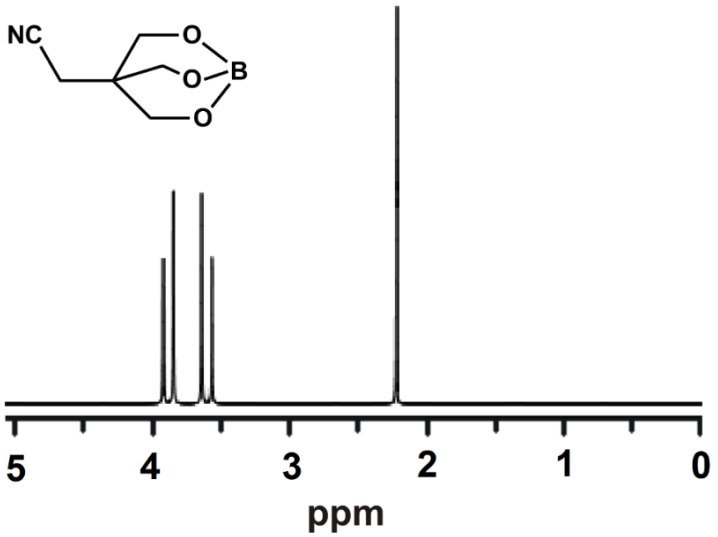

Figure A.7 : ^{1}H NMR Spectrum of 2-(2,6,7-trioxa-1-borabicyclo[2.2.2]octan-4-yl)acetonitrile

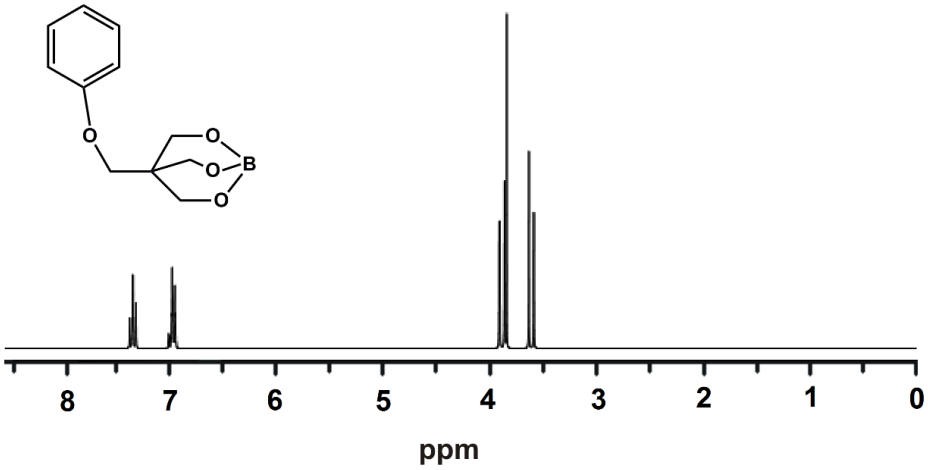

Figure A.8 : ^{1}H NMR Spectrum of 4-(phenoxymethyl)-2,6,7-trioxa-1-borabicyclo[2.2.2]octane

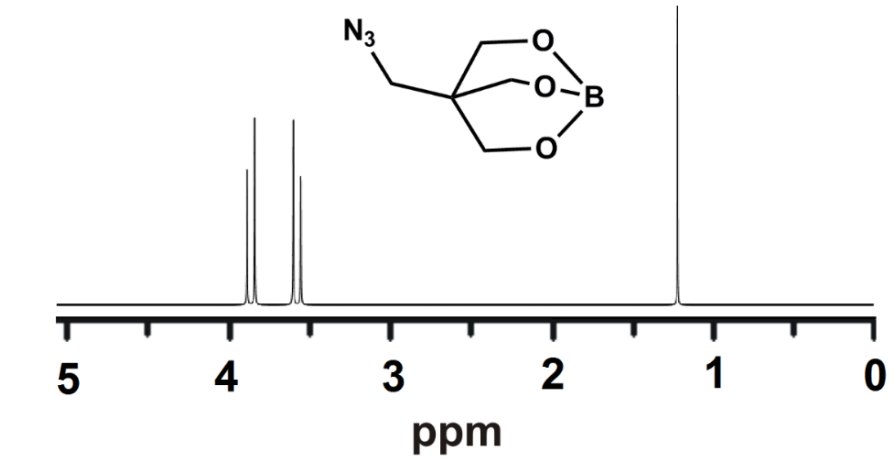

Figure A.9 : ^{1}H NMR Spectrum of 4-(azidomethyl)-2,6,7-trioxa-1-borabicyclo[2.2.2]octane

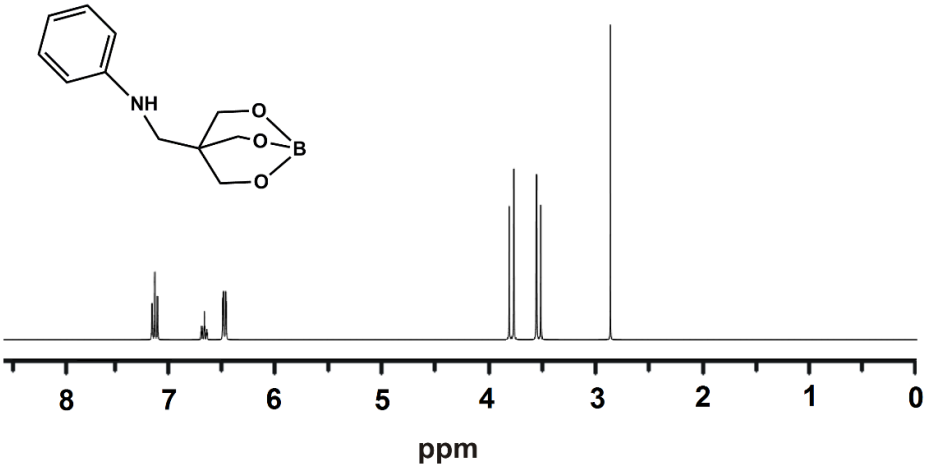

Figure A.10 : ^{1}H NMR Spectrum of *N*-(2,6,7-trioxa-1-borabicyclo[2.2.2]octan-4-ylmethyl)aniline

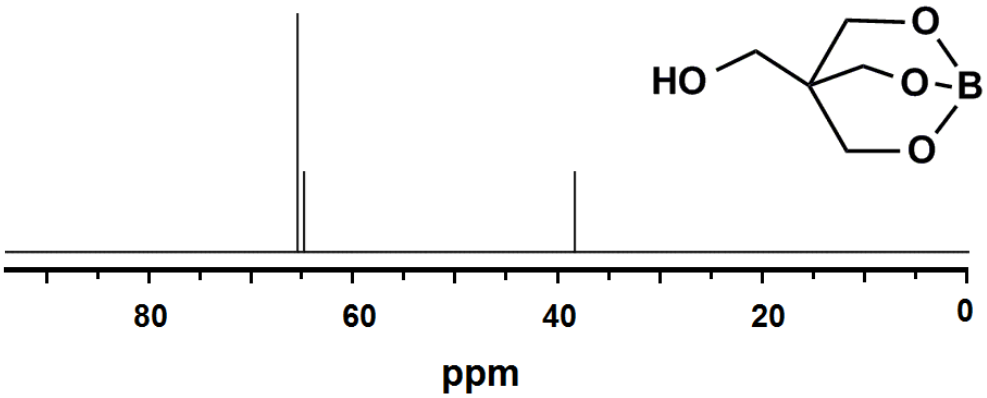

Figure A.11 : ^{13}C NMR Spectrum of boron chelated pentaerythritol [2,6,7-trioxa-1-borabicyclo[2.2.2]octan-4-ylmethanol]

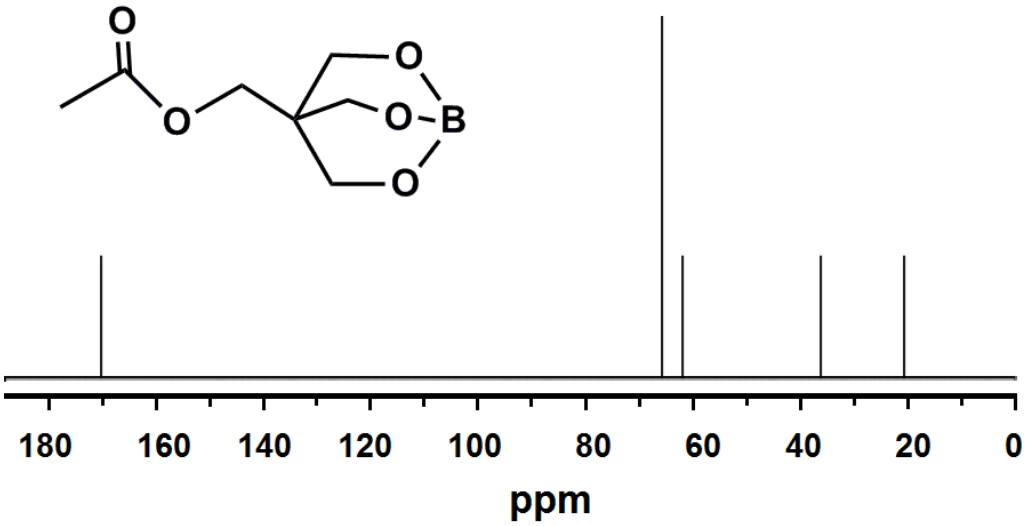

Figure A.12 : ^{13}C NMR Spectrum of boron chelated pentaerythritol monoacetate [2,6,7-trioxa-1-borabicyclo[2.2.2]octan-4-ylmethyl acetate]

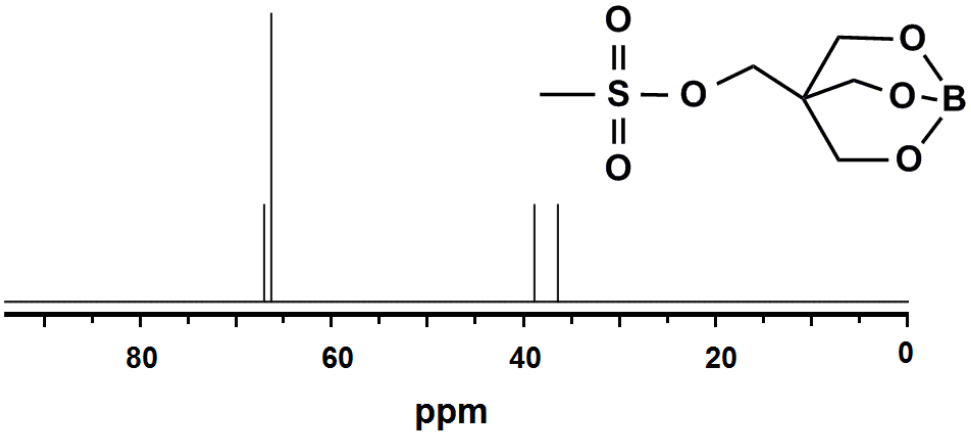

Figure A.13 : ^{13}C NMR Spectrum of boron chelated pentaerythritol monomesylate [2,6,7-trioxa-1-borabicyclo[2.2.2]octan-4-ylmethyl methanesulfonate]

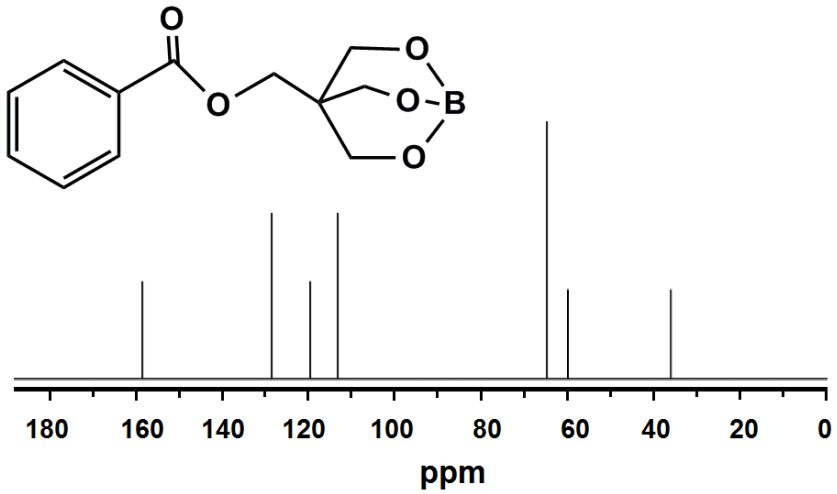

Figure A.14 : ^{13}C NMR Spectrum of 4-(phenoxymethyl)-2,6,7-trioxa-1-borabicyclo[2.2.2]octane

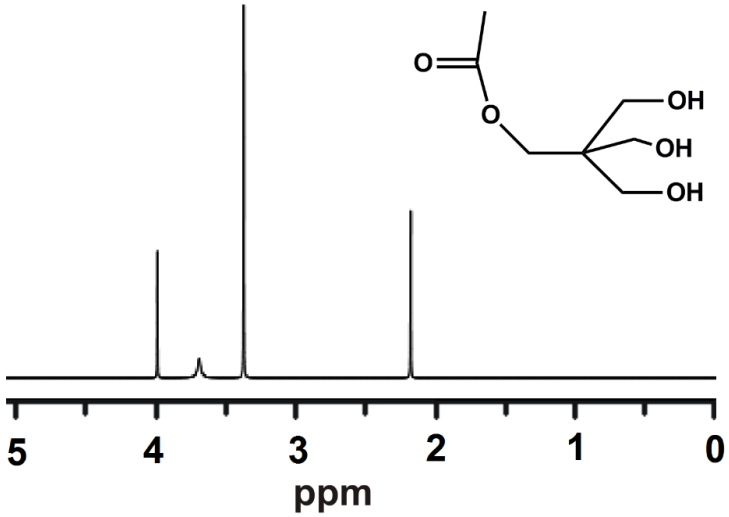

Figure A.15 : ^{1}H NMR Spectrum of pentaerythritol monoacetate [3-hydroxy-2,2-bis(hydroxymethyl)propyl acetate]

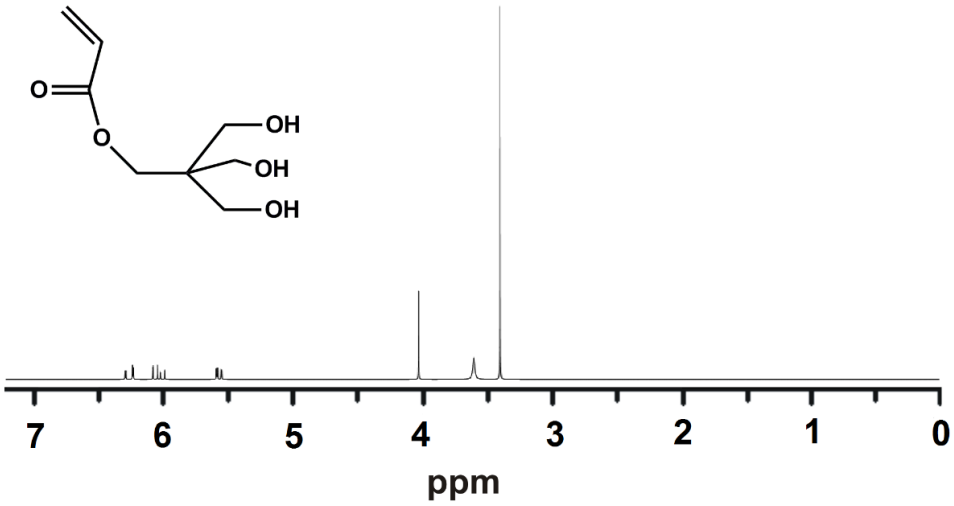

Figure A.16 : ^{1}H NMR Spectrum of pentaerythritol monoacrylate [3-hydroxy-2,2-bis(hydroxymethyl)propyl acrylate]

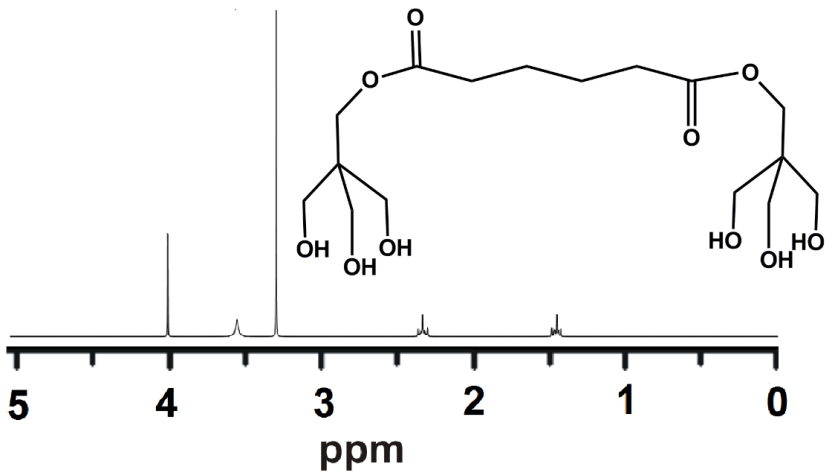

Figure A.17 : ^{1}H NMR Spectrum of dipentaerythritol monoadipate [bis(3-hydroxy-2,2-bis(hydroxymethyl)propyl) adipate]

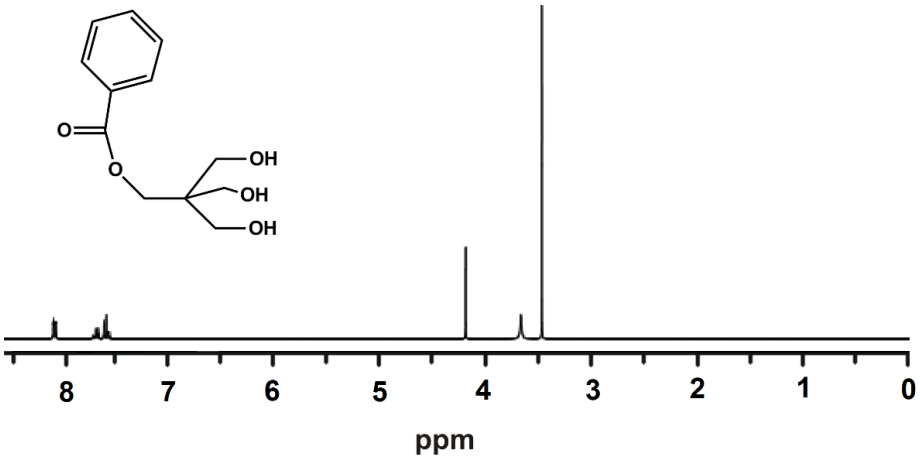

Figure A.18 : ^{1}H NMR Spectrum of pentaerythritol monobenzoate [3-hydroxy-2,2-bis(hydroxymethyl)propyl benzoate]

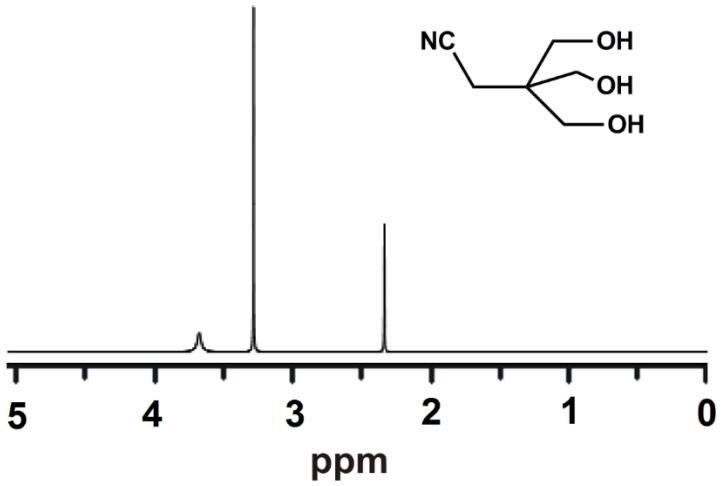

Figure A.19 : ^{1}H NMR Spectrum of 4-hydroxy-3,3-bis(hydroxymethyl)butanenitrile

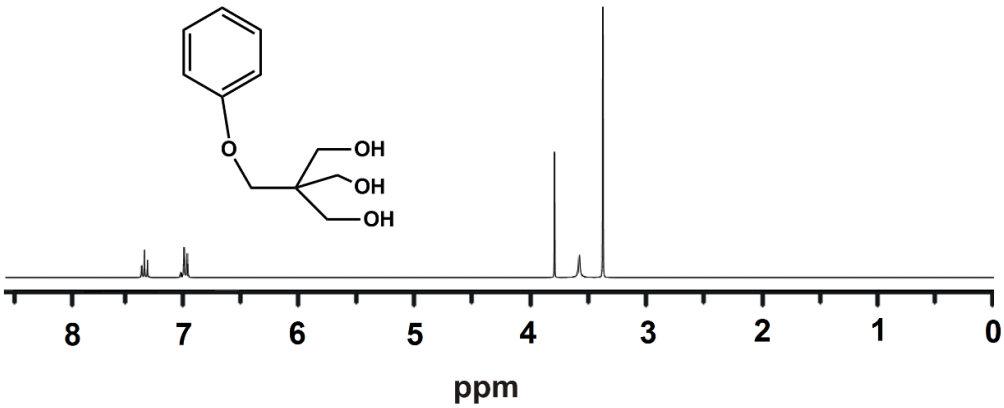

Figure A.20 : ^{1}H NMR Spectrum of 2-(hydroxymethyl)-2-(phenoxymethyl)propane-1,3-diol

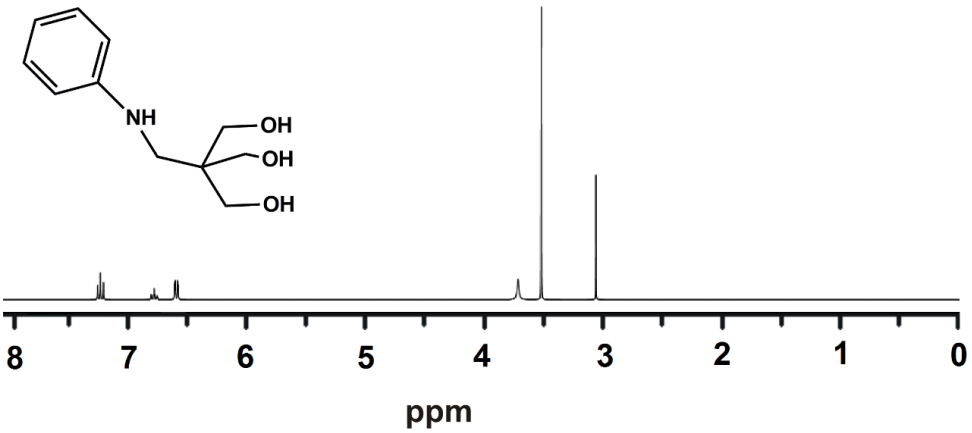

Figure A.21 : ^{1}H NMR Spectrum of 2-(hydroxymethyl)-2-((phenylamino)methyl)propane-1,3-diol

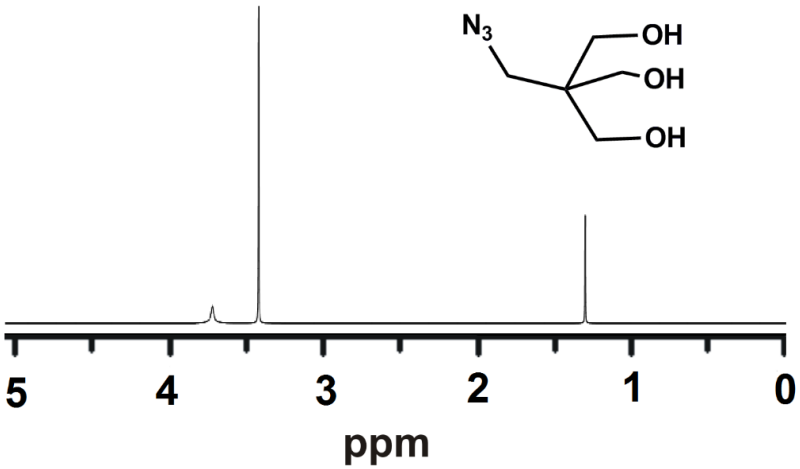

Figure A.22 : ^{1}H NMR Spectrum of 2-(azidomethyl)-2-(hydroxymethyl)propane-1,3-diol

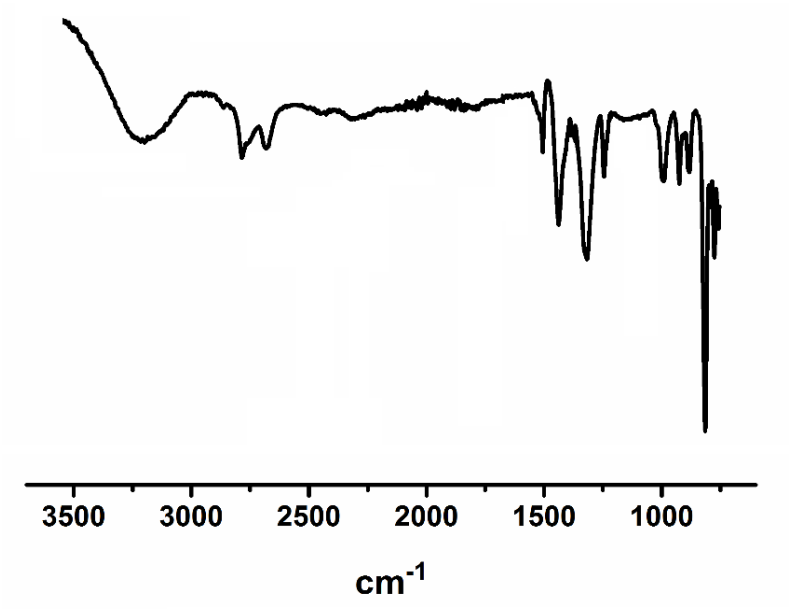

Figure A.23 : FT-IR Spectrum of boron chelated pentaerythritol [2,6,7-trioxa-1-borabicyclo[2.2.2]octan-4-ylmethanol]

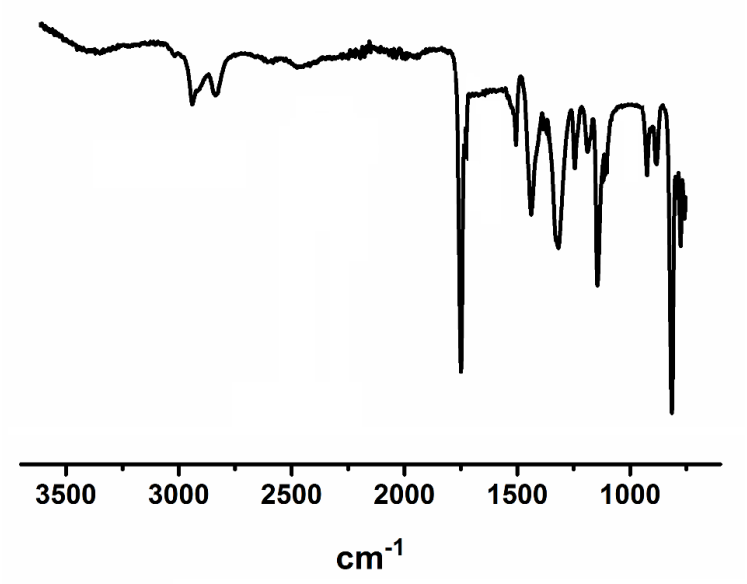

Figure A.24 : FT-IR Spectrum of boron chelated pentaerythritol monoacetate [2,6,7-trioxa-1-borabicyclo[2.2.2]octan-4-ylmethyl acetate]

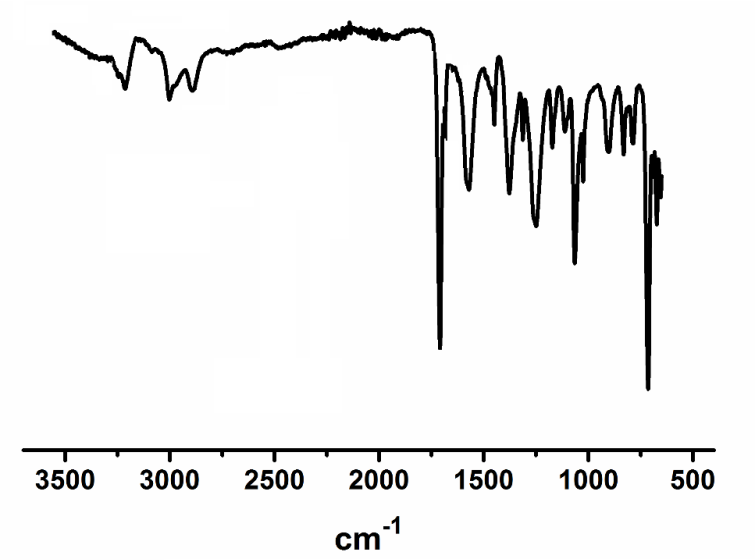

Figure A.25 : FT-IR Spectrum of boron chelated pentaerythritol monoacrylate [2,6,7-trioxa-1-borabicyclo[2.2.2]octan-4-ylmethyl acrylate]

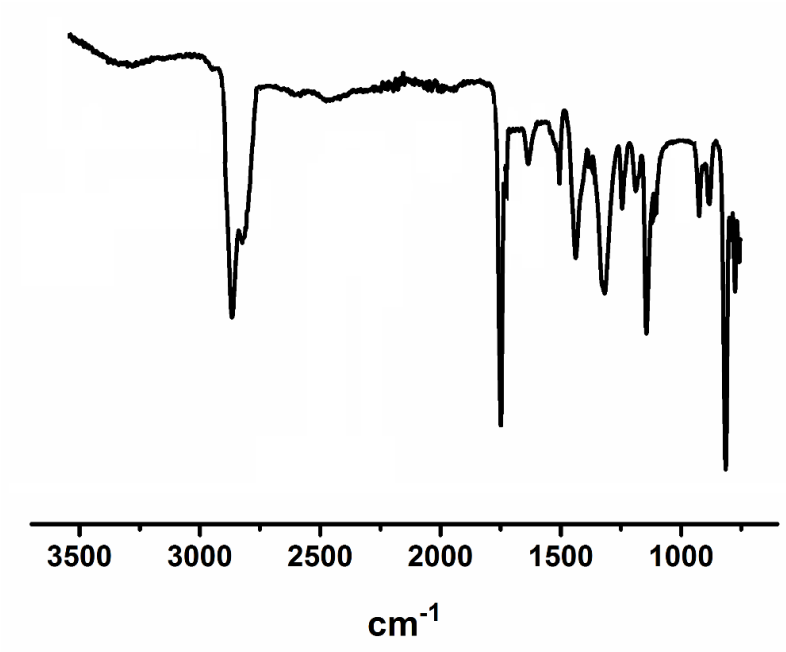

Figure A.26 : FT-IR Spectrum of boron chelated dipentaerythritol monoadipate [bis(2,6,7-trioxa-1-borabicyclo[2.2.2]octan-4-ylmethyl) adipate]

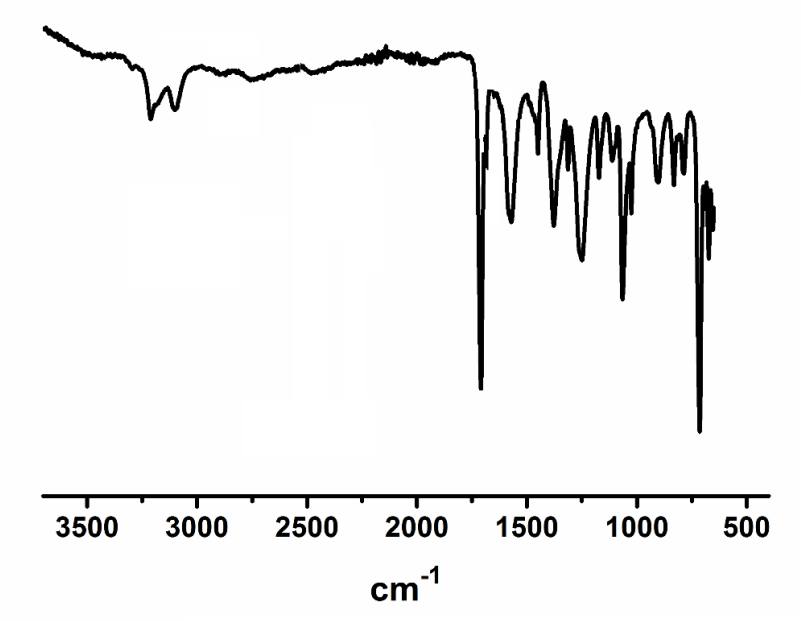

Figure A.27 : FT-IR Spectrum of boron chelated pentaerythritol monobenzoate [2,6,7-trioxa-1-borabicyclo[2.2.2]octan-4-ylmethyl benzoate]

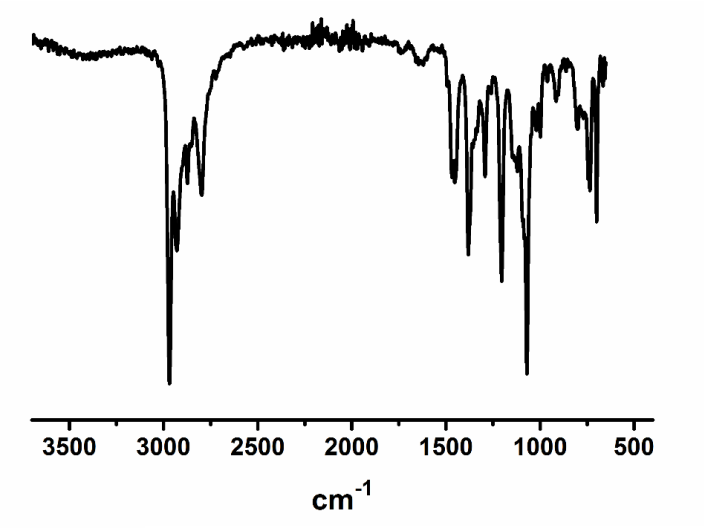

Figure A.28 : FT-IR Spectrum of boron chelated pentaerythritol monomesylate [2,6,7-trioxa-1-borabicyclo[2.2.2]octan-4-ylmethyl methanesulfonate]

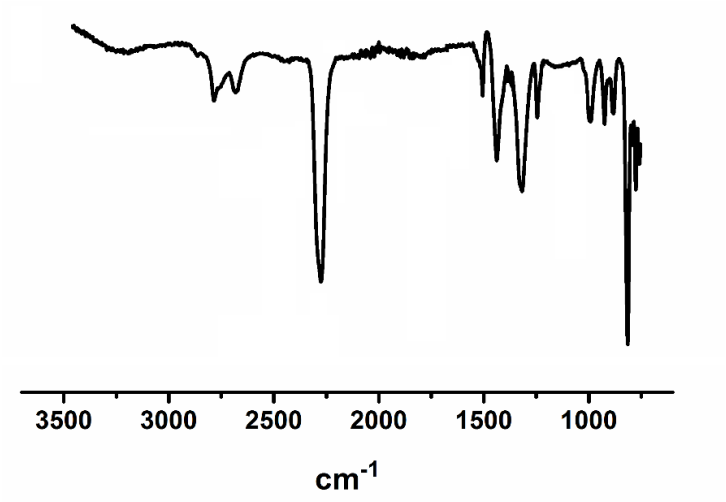

Figure A.29 : FT-IR Spectrum of 2-(2,6,7-trioxa-1-borabicyclo[2.2.2]octan-4-yl)acetonitrile

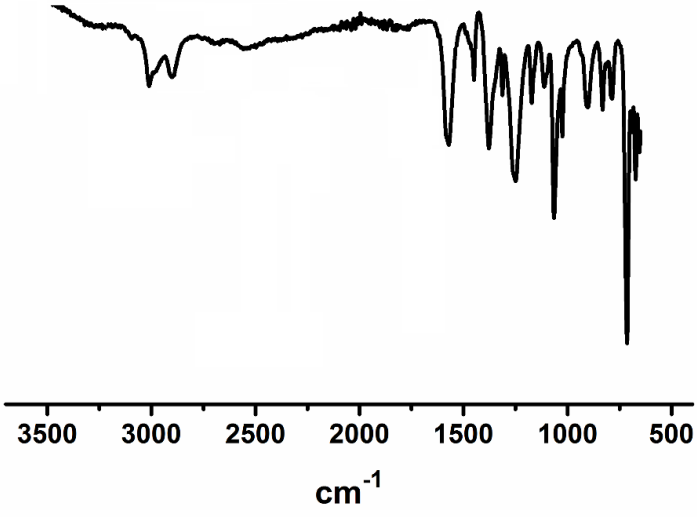

Figure A.30 : FT-IR Spectrum of 4-(phenoxymethyl)-2,6,7-trioxa-1-borabicyclo[2.2.2]octane

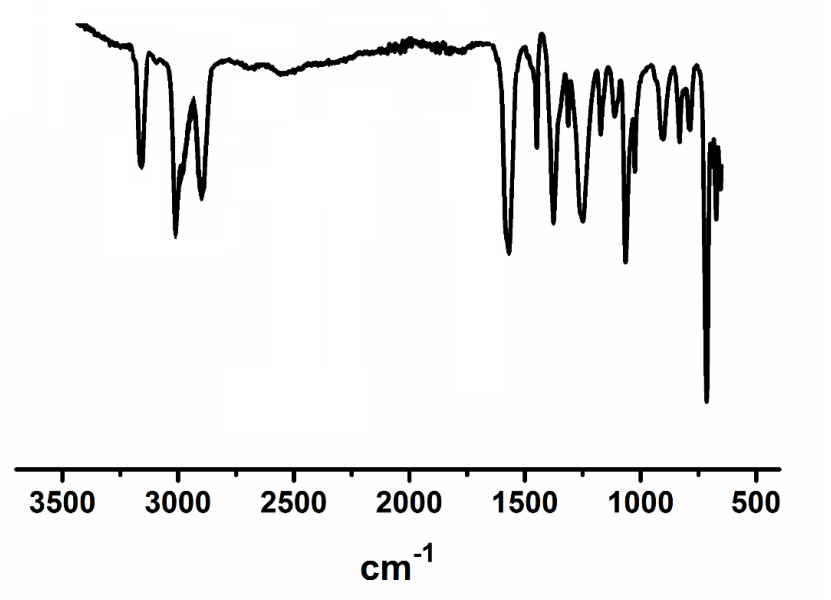

Figure A.31 : FT-IR Spectrum of *N*-(2,6,7-trioxa-1-borabicyclo[2.2.2]octan-4-ylmethyl)aniline

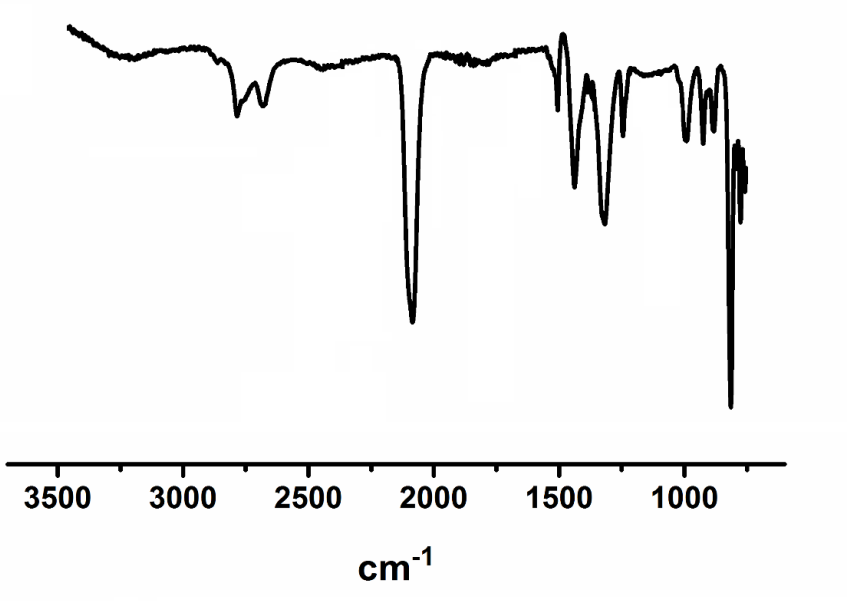

Figure A.32 : FT-IR Spectrum of 4-(azidomethyl)-2,6,7-trioxa-1-borabicyclo[2.2.2]octane

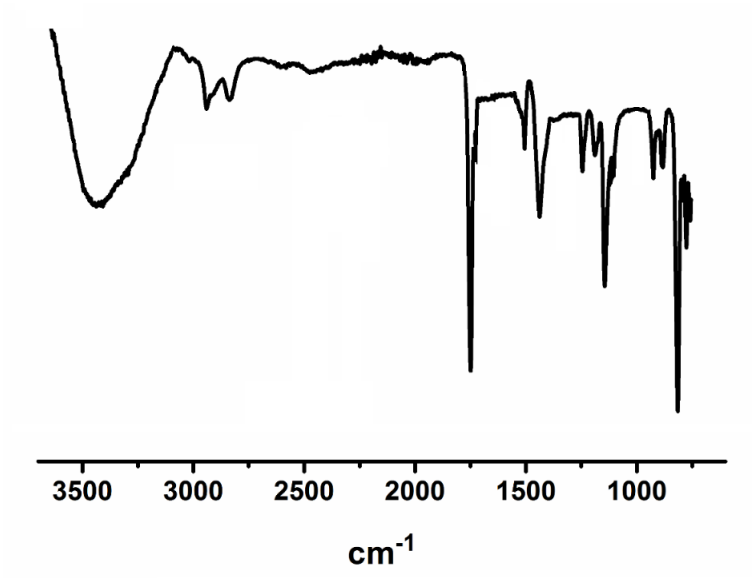

Figure A.33 : FT-IR Spectrum of pentaerythritol monoacetate [3-hydroxy-2,2-bis(hydroxymethyl)propyl acetate]

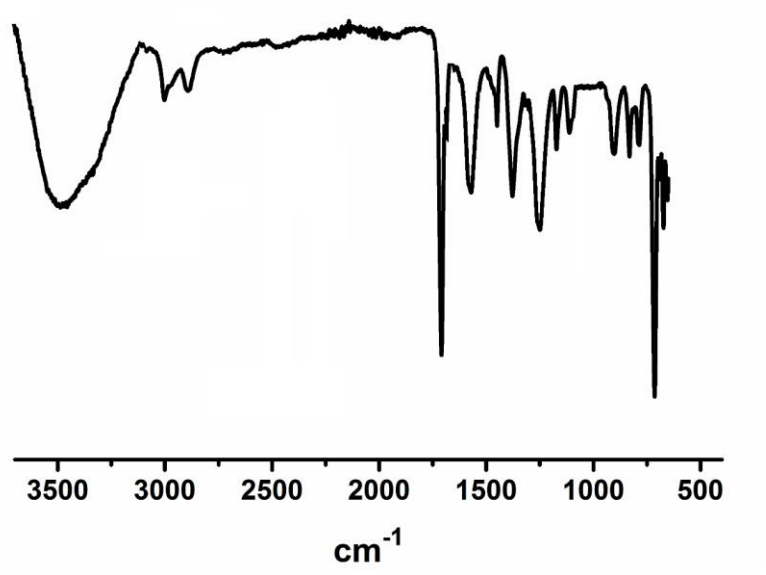

Figure A.34 : FT-IR Spectrum of pentaerythritol monoacrylate [3-hydroxy-2,2-bis(hydroxymethyl)propyl acrylate]

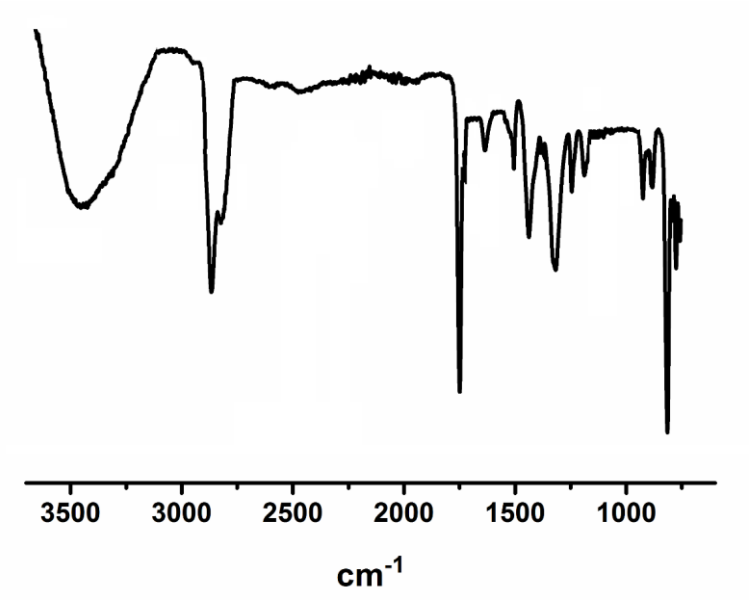

Figure A.35 : FT-IR Spectrum of dipentaerythritol monoadipate [bis(3-hydroxy-2,2-bis(hydroxymethyl)propyl) adipate]

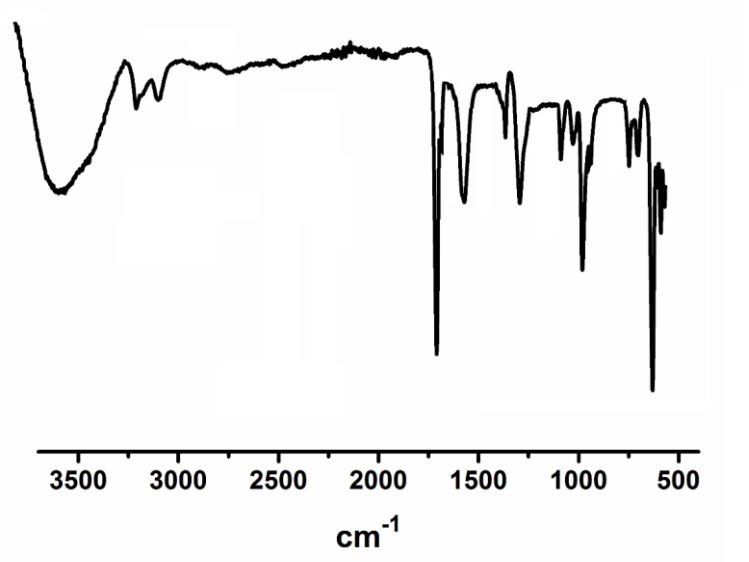

Figure A.36 : FT-IR Spectrum of pentaerythritol monobenzoate [3-hydroxy-2,2-bis(hydroxymethyl)propyl benzoate]

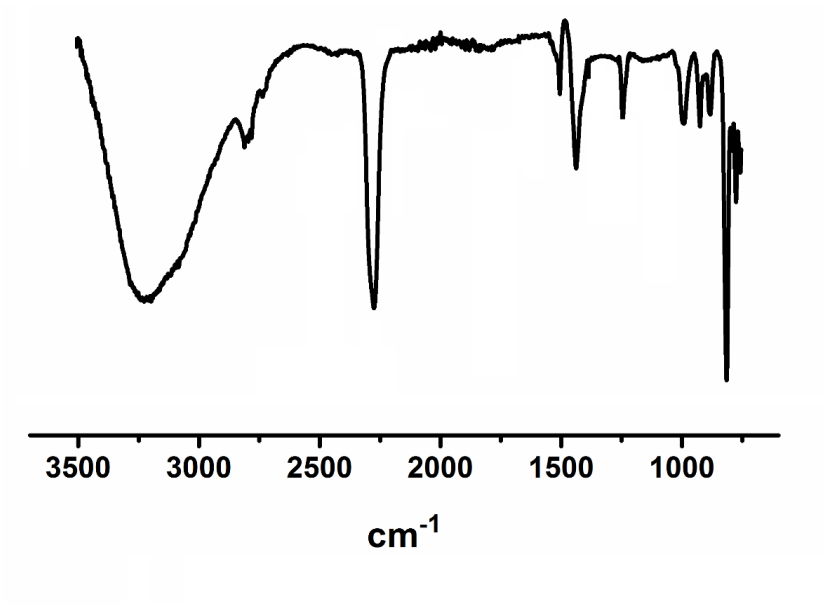

Figure A.37 : FT-IR Spectrum of 4-hydroxy-3,3-bis(hydroxymethyl)butanenitrile

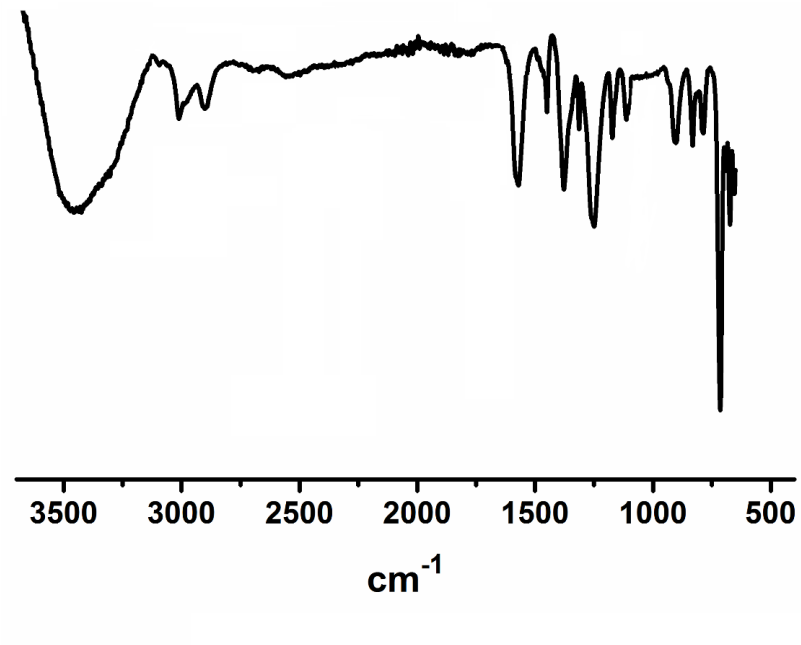

Figure A.38 : FT-IR Spectrum of 2-(hydroxymethyl)-2-(phenoxymethyl)propane-1,3-diol

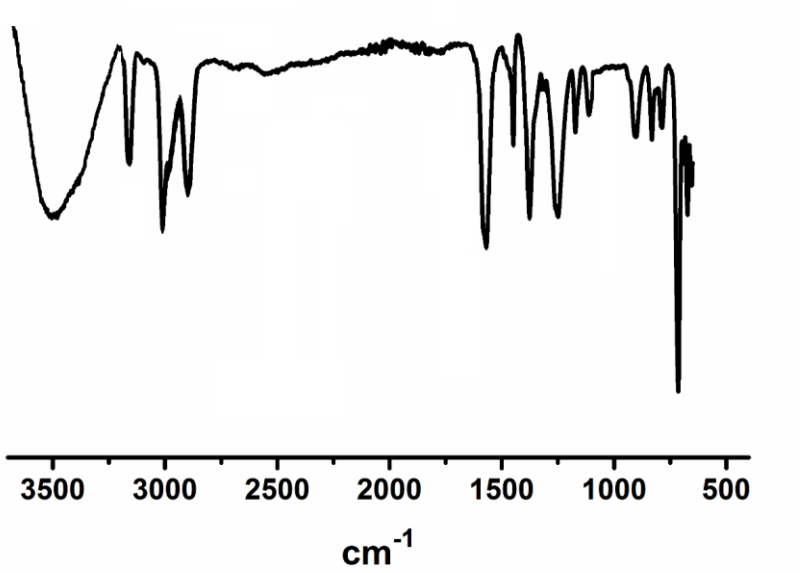

Figure A.39 : FT-IR Spectrum of 2-(hydroxymethyl)-2-((phenylamino)methyl)propane-1,3-diol

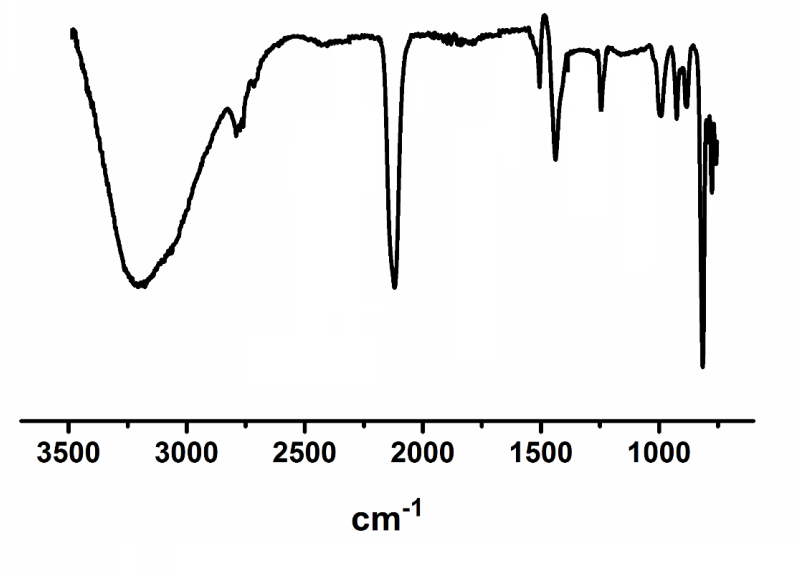

Figure A.40 : FT-IR Spectrum of 2-(azidomethyl)-2-(hydroxymethyl)propane-1,3-diol

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ARTICLES, PRESENTATIONS AND PATENTS:

- Kumru, B., Gure, B., Bicak, N., 2013. Regio-selective peroxybromination of poly (vinyl methyl ketone) as versatile tool for generation active ATRP initiation sites on solid surfaces *Journal of Polymer Science: Part A Polymer Chemistry*, 51 (18), 3892-3900

- Kumru, B., Bicak, N., 2015. Synthesis of soluble poly(vinylene carbonate) by redox-initiated RAFT process in microemulsion and its aminolysis yielding snow-white polymethylol *RSC Advances*, 5, 30936

- Kumru, B., Bicak, N., 2015. Polymerization of Aniline by Catalytic Air Oxidation in Microemulsion *Macromolecular Symposia*, 352, 42–45

- Selective Synthesis of Mono-substituted Pentaerythritols via Bicyclic Neutral Boron Ester Formation, Submitted to *Organic Chemistry Frontiers*

- Manufacturing Of Mono Methacrylate Functional Pentaerythritol Monomer And Its High Capacity Boron Specific Polymers, Submitted to *Macromol. Chem. Phys.*

- Kumru, B., Bicak, N., 2015. An unusual Approach to Yield poly(allyl amine) *via* Hydrolysis of Poly(allyl acetaldimine), *International Congress - EPF 2015*, June 21-26, 2015 Dresden, Germany

- Kumru, B., Bicak, N., 2014. Polymerization of Aniline by Catalytic Air Oxidation, *International Congress – POC 2014*, June 10-13, 2014 Timişoara, Romania

- Kumru, B., Bicak, N., 2013. Facile method for bromomethylsilanation of silica microspheres for further modification, *International Congress – IUPAC 2013*, August 11-16, 2013 Istanbul, Turkey

- Kumru, B., Bicak, N., 2013. Defect-free polymers via redox-initiated RAFT polymerization of vinylene carbonate at room temperature, *International Congress - EPF 2013*, June 16-21, 2013 Pisa, Italy